

=> s H1(1)H3

25581 H1

19234 H3

L1 2855 H1(L)H3

=> s l1 and allerg?

69227 ALLERG?

L2 93 L1 AND ALLERG?

=> s l2 and (loratadine or desloratadine or dsl)

923 LORATADINE

304 DESLORATADINE

368 DSL

L3 17 L2 AND (LORATADINE OR DESLORATADINE OR DSL)

=> d bib hit 1-17

L3 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:740597 CAPLUS

DN 145:188876

TI Preparation of imidazole and benzimidazole derivatives as histamine H3 antagonists

IN Aslanian, Robert G.; Tom, Wing C.; Zhu, Xiaohong

PA Schering Corporation, USA

SO PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006078775	A1	20060727	WO 2006-US1832	20060119
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

US 2006166960	A1	20060727	US 2006-334932	20060119
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PRAI US 2005-646094P P 20050121

OS MARPAT 145:188876

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The title compds. I [n = 2-5; R = is R3-aryl, R3-heteroaryl, R3-cycloalkyl, R3-heterocycloalkyl, alkyl, haloalkyl, -OR4, -SR4 or -S(O)1-2R5; R1 = H and R2 = H or (un)substituted Ph or pyridyl, or R1 = H or (un)substituted Ph or pyridyl and R2 = H, and X = O or S; or R1 and R2, together with the carbon atoms to which they are attached, form (un)substituted fused benzo or pyrido ring, and X = O, S or NR7; Z = (un)substituted pyrrolidino, piperidino, piperazino, etc.; R3 = H, alkyl, halo, etc.; R4 = alkyl, arylalkyl or cycloalkyl; R5 = alkyl, R3-aryl, R3-arylalkyl, etc.; R7 = H, alkyl, etc.], useful as histamine H3 antagonists, were prepared. For example, a multistep synthesis of II, starting from 4-aminophenol and 2,5-difluoronitrobenzene, was given (no characterization data for intermediates). II showed Ki of 1 nM in H3 receptor binding assay. Also disclosed are pharmaceutical compns. comprising the compds. I, methods of treating allergy,

allergy-induced airway responses, congestion, obesity and metabolic syndrome using the compds. I , as well as combinations with other drugs useful for treating those diseases.

ST imidazole prepn histamine H3 antagonist combination chemotherapy allergy inhibitor; benzimidazole prepn histamine H3 antagonist combination chemotherapy allergy inhibitor

IT Antihistamines  
(H1; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Histamine receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(H1; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Antihistamines  
(H3; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Histamine receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(H3; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Mental and behavioral disorders  
(attention deficit hyperactivity disorder; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Drug delivery systems  
(carriers; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Nose, disease  
(congestion; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Gastrointestinal motility  
(disorder, dysmotility; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Central nervous system, disease  
(hyperactivity; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Respiratory system, disease  
(hyperresponsiveness, allergy-induced airway response; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Central nervous system, disease  
(hypoactivity; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Metabolic disorders  
(metabolic syndrome X; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Headache  
(migraine; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Allergy  
Allergy inhibitors  
Alzheimer's disease  
Anti-Alzheimer's agents  
Antihypotensives  
Antimigraine agents  
Antiobesity agents  
Antipsychotics  
Cardiovascular agents  
Cardiovascular system, disease  
Central nervous system, disease  
Central nervous system agents  
Combination chemotherapy  
Digestive tract, disease  
Gastrointestinal agents  
Human  
Hypotension  
Nervous system stimulants  
Obesity  
Schizophrenia  
Sleep disorders  
(preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Gastric acid  
(secretion, hyperacidity; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Gastric acid  
(secretion, hypoacidity; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT Gastric acid  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(secretion, inhibitors; preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT 100643-71-8  
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT 902780-36-3P 902780-37-4P 902780-38-5P 902780-39-6P 902780-40-9P  
902780-41-0P 902780-42-1P 902780-43-2P 902780-44-3P 902780-45-4P  
902780-46-5P 902780-47-6P 902780-48-7P 902780-49-8P 902780-50-1P  
902780-51-2P 902780-52-3P 902780-53-4P 902780-54-5P 902780-55-6P  
902780-56-7P 902780-57-8P 902780-58-9P 902780-59-0P 902780-60-3P  
902780-61-4P 902780-62-5P 902780-63-6P 902780-64-7P 902780-65-8P  
902780-66-9P 902780-67-0P 902780-68-1P 902780-69-2P 902780-70-5P  
902780-71-6P 902780-72-7P 902780-73-8P 902780-74-9P 902780-75-0P  
902780-76-1P 902780-77-2P 902780-78-3P 902780-79-4P 902780-80-7P  
902780-81-8P 902780-82-9P 902780-83-0P 902780-84-1P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT 58-73-1, Diphenhydramine 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6 91-81-6, Tripeleminamine 91-84-9, Pyrilamine 129-03-3, Cyproheptadine 132-22-9, Chloropheniramine 469-21-6, Doxylamine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 569-65-3, Meclizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 15686-51-8, Clemastine 24219-97-4, Mianserin 29216-28-2, Mequitazine 34580-13-7, Ketotifen 39577-19-0, Picumast 50679-08-8, Terfenadine 58581-89-8, Azelastine 68844-77-9, Astemizole 75970-99-9, Norastemizole 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7, Epinastine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 90729-42-3, Carebastine 90729-43-4, Ebastine 108612-45-9, Mizolastine 110588-56-2, Noverastine 150756-35-7, Efenitidine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT 91-21-4, 1,2,3,4-Tetrahydroisoquinoline 92-54-6, 1-Phenylpiperazine 98-98-6, Picolinic acid 100-02-7, 4-Nitrophenol, reactions 109-01-3, 1-Methylpiperazine 109-70-6, 1-Bromo-3-chloropropane 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 111-49-9, Homopiperidine 119-53-9 123-30-8, 4-Aminophenol 123-75-1, Pyrrolidine, reactions 123-90-0, Thiomorpholine 141-91-3 177-11-7, 1,4-Dioxo-8-azaspiro[4.5]decane 364-74-9, 2,5-Difluoronitrobenzene 496-12-8 504-78-9, Thiazolidine 2293-07-4 2759-28-6, 4-Benzylpiperazine 2971-79-1, Methyl piperidine-4-carboxylate 3367-95-1 4138-26-5, 3-Piperidinecarboxamide 4318-37-0 4410-12-2 4897-50-1, 4-Piperidinopiperidine 5004-07-9, 4-Pyrrolidinopiperidine 5382-16-1, 4-Hydroxypiperidine 5472-49-1, 1-(3-Chloropropyl)piperidine hydrochloride 13889-98-0, 1-Acetylpiperazine 17766-28-8, 1-Cyclohexylpiperazine 22817-26-1 31166-44-6 31252-42-3, 4-Benzylpiperidine 34803-66-2, 1-(2-Pyridyl)piperazine 35794-11-7, 3,5-Dimethylpiperidine 39546-32-2, 4-Piperidinecarboxamide 39713-72-9 40004-08-8 40172-95-0 40499-83-0, 3-Hydroxypyrrolidine 57260-71-6, tert-Butyl piperazine-1-carboxylate 68377-27-5 79286-74-1 132958-72-6 902780-85-2 902780-86-3 902780-87-4 902780-88-5 902780-89-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

IT 79096-54-1P 79713-63-6P 92374-75-9P 251552-34-8P 902780-90-9P 902780-91-0P 902780-92-1P 902780-93-2P 902780-94-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of imidazole and benzimidazole derivs. as histamine H3 antagonists for treating allergy, allergy-induced airway responses, congestion, obesity and metabolic syndrome)

L3 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:684424 CAPLUS

DN 145:224201

TI Stimulating effects of H1-antagonists

AU Theunissen, Eef L.; Vermeeren, Annemiek; Vuurman, Eric F. P. M.; Ramaekers, Johannes G.

CS Experimental Psychopharmacology Unit, Brain and Behavior Institute, Faculty of Psychology, Maastricht University, Neth.

SO Current Pharmaceutical Design (2006), 12(20), 2501-2509

CODEN: CPDEFP; ISSN: 1381-6128

PB Bentham Science Publishers Ltd.

DT Journal; General Review

LA English

RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A review. Whereas antihistamines are generally known for their sedative side effects, this review shows that several studies also found mild stimulating effects on performance for the H1-antagonists terfenadine, ebastine, fexofenadine and desloratadine. These stimulating effects were mostly demonstrated in tasks involving high levels of attention, e.g. divided attention tasks, vigilance tasks and driving tasks. The stimulating effects of these antihistamines were often dependent of the given dose; however the relation was not always linear. The mechanism responsible for the stimulating effects of these four antihistamines is still unclear, though it is hypothesized that it involves other neurotransmitters like dopamine and GABA, or that it acts through the H3 histamine receptor. Further research is needed to clarify the ambiguous role of histamine in processes of arousal. In addition, it would be useful to determine whether terfenadine, ebastine, fexofenadine and desloratadine can return allergic patient's performance back to their preclin. level.

IT Histamine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (H3; stimulating effects of H1-antagonists)

IT 50679-08-8, Terfenadine 83799-24-0, Fexofenadine 90729-43-4, Ebastine 100643-71-8, Desloratadine

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (stimulating effects of H1-antagonists)

L3 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:675663 CAPLUS

DN 141:185095

TI Use of combinations of H1 and H3 histamine receptor antagonists for the preparation of a medicament for the treatment of allergic skin and allergic ocular conditions

IN Hey, John A.; Kreutner, William; McLeod, Robbie L.

PA Schering Corporation, USA

SO PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004069338	A1	20040819	WO 2004-US2370	20040129
	W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004198743	A1	20041007	US 2004-767164	20040129

PRAI US 2003-443948P P 20030131

TI Use of combinations of H1 and H3 histamine receptor antagonists for the preparation of a medicament for the treatment of allergic skin and allergic ocular conditions

AB The invention provides methods for treating allergic skin and

ocular conditions and disorders by combined administration of an histamine H1 receptor antagonist and a histamine H3 receptor antagonist.

- ST histamine H1 H3 antagonist combination eye skin allergy treatment
- IT Antihistamines
  - (H1; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Antihistamines
  - (H3; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Allergy
  - Eye, disease
  - Inflammation
    - (allergic conjunctivitis; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Drug delivery systems
  - (capsules; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Allergy
  - Allergy inhibitors
  - Antibiotics
  - Combination chemotherapy
  - Drug delivery systems
  - Drug interactions
  - Drug screening
  - Eye, disease
  - Hay fever
  - Human
  - Skin, disease
  - Urticaria
    - (combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Steroids, biological studies
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Eye, disease
  - Inflammation
    - (conjunctivitis; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Eye, disease
  - Inflammation
    - (keratoconjunctivitis; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Anti-inflammatory agents
  - (nonsteroidal; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Drug delivery systems
  - (parenterals; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)
- IT Blood vessel
  - (permeability, microvascular permeability; combinations of H1

and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)

IT Biological transport  
(permeation, vascular, microvascular permeability; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)

IT Drug delivery systems  
(tablets; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)

IT Drug delivery systems  
(topical; combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)

IT 58-73-1, Diphenhydramine 59-33-6, Pyrillamine 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6, Brompheniramine 91-81-6, Tripeleminamine 113-92-8, Chlorpheniramine maleate 129-03-3, Cyproheptadine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 523-87-5, Dimenhydrinate 562-10-7, Doxylamine 569-65-3, Meclizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 5786-21-0, Clozapine 15686-51-8, Clemastine 24219-97-4, Mianserin 24934-49-4 29216-28-2, Mequitazine 34580-13-7, Ketotifen 34970-69-9, Burimamide 34973-91-6, Impentamine 39577-19-0, Picumast 50679-08-8, Terfenadine 55273-05-7, Impromidine 58581-89-8, Azelastine 68844-77-9, Astemizole 75970-99-9, Norastemizole 79313-75-0 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7, Epinastine 83184-43-4, Mifentidine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 90729-42-3 90729-43-4, Ebastine 99616-14-5, S-Sopromidine 100643-71-8, Desloratadine 106243-16-7, Thioperamide 108612-45-9, Mizolastine 110588-56-2, Noberastine 145231-35-2, Clobenpropit dihydrobromide 145231-45-4 148440-81-7, Thioperamide maleate 150756-35-7, Eflertirizine 184025-18-1, Ciproxifan 203180-53-4 203184-70-7 203184-71-8 203184-72-9 214283-29-1 224168-30-3 224168-31-4 224168-46-1 224585-45-9 224825-10-9 230968-41-9 405551-48-6 433976-18-2 459783-23-4 459783-24-5 459783-25-6 459783-26-7 459783-27-8 459783-28-9 459783-29-0 459783-30-3 459783-31-4 459783-32-5 618892-76-5 732280-39-6 732280-43-2 732280-45-4 732280-50-1 732280-54-5 732280-56-7 732280-58-9 732280-65-8 737757-49-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combinations of H1 and H3 histamine receptor antagonists for treatment of allergic skin and allergic ocular conditions)

L3 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:648353 CAPLUS

DN 141:167797

TI Combination of H1, H3 and H4 receptor antagonists for treatment of allergic and non-allergic pulmonary inflammation, congestion and allergic rhinitis

IN Anthes, John C.; West, Robert E.; Hey, John A.; Aslanian, Robert G.

PA Schering Corporation, USA

SO PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004066960	A2	20040812	WO 2004-US3565	20040126
	WO 2004066960	A3	20041021		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,  
 BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,  
 CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,  
 ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,  
 IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,  
 LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,  
 MZ, MZ, NA, NI

US 2005090527 A1 20050428 US 2004-764780 20040126

PRAI US 2003-443207P P 20030128

TI Combination of H1, H3 and H4 receptor antagonists for  
 treatment of allergic and non-allergic pulmonary  
 inflammation, congestion and allergic rhinitis

AB The invention includes methods for treating allergic conditions  
 involving the airway by administering histamine receptor antagonists.

ST histamine receptor antagonist allergic pulmonary inflammation  
 rhinitis

IT Histamine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (H1; combination of H1, H3 and H4  
 receptor antagonists for treatment of allergic and non-  
 allergic pulmonary inflammation, congestion and  
 allergic rhinitis)

IT Histamine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (H3; combination of H1, H3 and H4  
 receptor antagonists for treatment of allergic and non-  
 allergic pulmonary inflammation, congestion and  
 allergic rhinitis)

IT Histamine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (H4; combination of H1, H3 and H4 receptor  
 antagonists for treatment of allergic and non-  
 allergic pulmonary inflammation, congestion and  
 allergic rhinitis)

IT Allergy

Inflammation

Nose, disease

(allergic rhinitis; combination of H1, H3  
 and H4 receptor antagonists for treatment of allergic and  
 non-allergic pulmonary inflammation, congestion and  
 allergic rhinitis)

IT Inflammation

(allergic, pulmonary inflammation; combination of H1  
 , H3 and H4 receptor antagonists for treatment of  
 allergic and non-allergic pulmonary inflammation,  
 congestion and allergic rhinitis)

IT Drug delivery systems

(capsules; combination of H1, H3 and H4 receptor  
 antagonists for treatment of allergic and non-  
 allergic pulmonary inflammation, congestion and  
 allergic rhinitis)

IT Anti-inflammatory agents

Drug screening

Human

Inflammation

Respiratory system

(combination of H1, H3 and H4 receptor antagonists  
 for treatment of allergic and non-allergic  
 pulmonary inflammation, congestion and allergic rhinitis)

IT Allergy

(inflammation, pulmonary inflammation; combination of H1,  
 H3 and H4 receptor antagonists for treatment of  
 allergic and non-allergic pulmonary inflammation,  
 congestion and allergic rhinitis)



IT Drug delivery systems  
(parenterals; combination of H1, H3 and H4 receptor antagonists for treatment of allergic and non-allergic pulmonary inflammation, congestion and allergic rhinitis)

IT Drug interactions  
(pharmacodynamic; combination of H1, H3 and H4 receptor antagonists for treatment of allergic and non-allergic pulmonary inflammation, congestion and allergic rhinitis)

IT Inflammation  
Lung, disease  
(pneumonitis, allergic and non-allergic; combination of H1, H3 and H4 receptor antagonists for treatment of allergic and non-allergic pulmonary inflammation, congestion and allergic rhinitis)

IT Drug delivery systems  
(tablets; combination of H1, H3 and H4 receptor antagonists for treatment of allergic and non-allergic pulmonary inflammation, congestion and allergic rhinitis)

IT 51-45-6, Histamine, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(combination of H1, H3 and H4 receptor antagonists for treatment of allergic and non-allergic pulmonary inflammation, congestion and allergic rhinitis)

IT 59-33-6, Pyrilamine 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6 91-81-6, Tripeleminamine 113-92-8, Chlorpheniramine 129-03-3, Cyproheptadine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 562-10-7, Doxylamine 569-65-3, Meclizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 5786-21-0, Clozapine 15686-51-8, Clemastine 24219-97-4, Mianserin 24934-49-4 29216-28-2, Mequitazine 34580-13-7, Ketotifen 34970-69-9, Burimamide 34973-91-6, Impentamine 39577-19-0, Picumast 50679-08-8, Terfenadine 55273-05-7, Impromidine 58581-89-8, Azelastine 68844-77-9, Astemizole 75970-99-9, Norastemizole 79313-75-0, Sopromidine 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7, Epinastine 83184-43-4, Mifentidine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 90729-42-3 90729-43-4, Ebastine 99616-14-5, S-Sopromidine 100643-71-8, Desloratadine 106243-16-7, Thioperamide 108612-45-9, Mizolastine 110588-56-2, Noberastine 145231-45-4 150756-35-7, Eflzetirizine 153259-65-5, SB207499 184025-18-1, Ciproxifan 203180-53-4 203184-70-7 203184-71-8 203184-72-9 214283-29-1 224168-30-3 224168-31-4 224168-46-1 224585-45-9 230968-41-9 405551-48-6 433976-18-2 459783-23-4 459783-24-5 459783-25-6 459783-26-7 459783-27-8 459783-28-9 459783-29-0 459783-30-3 459783-31-4 459783-32-5 618892-76-5 732280-39-6 732280-43-2 732280-45-4 732280-50-1 732280-54-5 732280-56-7 732280-58-9 732280-63-6 732280-65-8 732280-67-0  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination of H1, H3 and H4 receptor antagonists for treatment of allergic and non-allergic pulmonary inflammation, congestion and allergic rhinitis)

L3 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2004:2876 CAPLUS  
DN 140:59522  
TI Preparation of indole derivatives as histamine H3 antagonists  
IN Aslanian, Robert G.; Berlin, Michael Y.; Mangiaracina, Pietro; McCormick, Kevin D.; Mutahi, Mwangi W.; Rosenblum, Stuart B.  
PA Schering Corporation, USA  
SO PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004000831	A1	20031231	WO 2003-US19619	20030620
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2489337	AA	20031231	CA 2003-2489337	20030620
	AU 2003243709	A1	20040106	AU 2003-243709	20030620
	US 2004019099	A1	20040129	US 2003-600674	20030620
	US 6951871	B2	20051004		
	EP 1539742	A1	20050615	EP 2003-761216	20030620
	EP 1539742	B1	20061108		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	CN 1662524	A	20050831	CN 2003-814717	20030620
	JP 2005531615	T2	20051020	JP 2004-516072	20030620
	ZA 2004010213	A	20051020	ZA 2004-10213	20041217
PRAI	US 2002-390987P	P	20020624		
	WO 2003-US19619	W	20030620		

OS MARPAT 140:59522

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Title compds. I [wherein R1 = (un)substituted indolyl or an aza derivative thereof; R2 = (un)substituted (hetero)aryl, quinolyl, heterocycloalkyl; R12, R13 = alkyl, hydroxyl, alkoxy, etc., or R13 = O; m = independently 0-3; n = 1-3; p = 1-3; q = 1-5; X = a bond or alkylene; Y = CO, CS, COCH2, etc.; Z = a bond, alkylene, alkenylene, CO, etc.; M1 = CH or N; M2 = CR3 or N; and salts or solvates thereof] were prepared as histamine H3 antagonists in treatment of H3 receptor related diseases. For example, reaction of II with 3-(4-piperidinyl)-2-(2-pyridinyl)indole, followed by deprotection and substitution with 2-chloromethylpyridine gave III, which showed 1.50 nM binding constant with histamine H3. Thus, I and their pharmaceutical compds., as well as in combination with H1 receptor antagonists, are useful as histamine H3 antagonists for the treatment of inflammatory diseases, allergic conditions and central nervous system disorders (no data).

IT Antihistamines

(H1, combination therapy agent; preparation of indole derivs. as histamine H3 antagonists)

IT Respiratory system, disease

(hyperresponsiveness, allergy-induced; preparation of indole derivs. as histamine H3 antagonists)

IT Allergy

Allergy inhibitors  
Alzheimer's disease  
Anti-Alzheimer's agents  
Antihypotensives  
Antimigraine agents  
Antiobesity agents  
Antipsychotics  
Cardiovascular agents  
Cardiovascular system, disease  
Central nervous system, disease  
Decongestants

Digestive tract, disease  
Drug delivery systems  
Gastrointestinal agents  
Hyperkinesia  
Hypokinesia  
Hypotension  
Nervous system agents  
Obesity  
Schizophrenia  
Sleep disorders

(preparation of indole derivs. as histamine H3 antagonists)

IT 58-73-1, Diphenhydramine 59-33-6, Pyrillamine maleate 60-87-7,  
Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8,  
Trimeprazine 86-22-6, Brompheniramine 91-81-6, Tripeleennamine  
113-92-8 129-03-3, Cyproheptadine 486-12-4, Triprolidine 486-16-8,  
Carbinoxamine 562-10-7 569-65-3, Meclizine 3964-81-6, Azatadine  
5636-83-9, Dimethindene 15686-51-8, Clemastine 24219-97-4, Mianserin  
29216-28-2, Mequitazine 34580-13-7, Ketotifen 39577-19-0, Picumast  
50679-08-8, Terfenadine 58581-89-8, Azelastine 68844-77-9, Astemizole  
75970-99-9, Norastemizole 79516-68-0, Levocabastine 79794-75-5,  
Loratadine 80012-43-7, Epinastine 83799-24-0, Fexofenadine  
83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine  
90729-42-3, Carebastine 90729-43-4, Ebastine 100643-71-8,  
Descarboethoxyloratadine 108612-45-9, Mizolastine 110588-56-2,  
Noberasine 150756-35-7, Eflerizine  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination therapy agent; preparation of indole derivs. as histamine H3  
antagonists)

L3 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:991348 CAPLUS

DN 140:27826

TI Preparation of 1-(4-piperidinyl)benzimidazolones as histamine H3  
antagonists

IN Ting, Pauline C.; Aslanian, Robert G.; Berlin, Michael Y.; Boyce,  
Christopher W.; Cao, Jianhua; Mangiaracina, Pietro; Mc, Cormick Kevin D.;  
Mutahi, Mwangi W.; Rosenblum, Stuart B.; Shih, Neng-yang; Solomon, Daniel  
M.; Tom, Wing C.; Zeng, Qingbei

PA Schering Corporation, USA

SO PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN. CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003103669	A1	20031218	WO 2003-US11696	20030416
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU,				
	ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD,				
	MG, MK, MN, MX, MZ, NI, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG,				
	SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				
	KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				
	FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,				
	BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2482551	AA	20031218	CA 2003-2482551	20030416
	AU 2003223631	A1	20031222	AU 2003-223631	20030416
	US 2004048843	A1	20040311	US 2003-414943	20030416
	US 2004097483	A1	20040520	US 2003-417391	20030416
	US 7105505	B2	20060912		
	EP 1494671	A1	20050112	EP 2003-719770	20030416
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

	CN 1658875	A	20050824	CN 2003-813780	20030416
	JP 2005529161	T2	20050929	JP 2004-510788	20030416
	ZA 2004007985	A	20051019	ZA 2004-7985	20041004
	JP 2006206603	A2	20060810	JP 2006-79808	20060322
PRAI	US 2002-373467P	P	20020418		
	US 2002-373731P	P	20020418		
	JP 2004-510788	A3	20030416		
	WO 2003-US11696	W	20030416		
OS	MARPAT 140:27826				

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Disclosed are histamine H3 antagonists I [a, b = 0-3; n = 1-3; p = 1-3 (with the proviso that when M2 = N, then p is not 1); r = 1-3 (with the proviso that when r = 2 or 3, then M2 = CR3 and p = 2 or 3); A = a bond, alkylene; M1 = CR3, N; M2 = CR3, N; Y = CO, CS, SO, SO2, etc.; Z = a bond, alkylene, alkenylene, CO, CH(CN), etc.; R1 = (un)substituted benzimidazolone, quinazolone, etc.; R2 = (un)substituted aryl or heteroaryl; R3 = H, halo, alkyl, OH, alkoxy; R12, R13 = alkyl, OH, alkoxy, etc.]. Synthesis of representative compds. I is described. Thus, amidation of the amine II with the acid III (prepns. given) afforded 80% the compound IV. The compds. I showed a Ki within the range of about 0.1 to about 1000 nM in H3-receptor binding assay. Also disclosed are pharmaceutical compns. comprising the compds. I. Also disclosed are methods of treating various diseases or conditions, such as, for example, allergy, allergy-induced airway responses, and congestion (e.g., nasal congestion) using the compds. of I. Also disclosed are methods of treating various diseases or conditions, such as, for example, allergy, allergy-induced airway responses, and congestion (e.g., nasal congestion) using the compds. I in combination with a H1 receptor antagonist.

IT Allergy inhibitors  
Anti-Alzheimer's agents  
Antihistamines  
Antihypotensives  
Antimigraine agents  
Antiobesity agents  
Antipsychotics  
Cardiovascular agents  
Human  
Nervous system agents

(preparation of 1-(4-piperidinyl)benzimidazolones as histamine H3 antagonists)

IT Allergy  
Alzheimer's disease  
Cardiovascular system, disease  
Central nervous system, disease  
Digestive tract, disease  
Hypotension  
Obesity  
Schizophrenia  
Sleep disorders  
(treatment of; preparation of 1-(4-piperidinyl)benzimidazolones as histamine H3 antagonists)

IT 58-73-1, Diphenhydramine 59-33-6, Pyrillamine maleate 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6, Brompheniramine 91-81-6, Tripeleennamine 113-92-8 129-03-3, Cyproheptadine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 562-10-7 569-65-3, Meclizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 15686-51-8, Clemastine 24219-97-4, Mianserin 29216-28-2, Mequitazine 34580-13-7, Ketotifen 39577-19-0, Picumast 50679-08-8, Terfenadine 58581-89-8, Azelastine 68844-77-9, Astemizole 75970-99-9, Norastemizole 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7, Epinastine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine

90729-42-3, Carebastine 90729-43-4, Ebastine 100643-71-8,  
 Descarboethoxyloratadine 108612-45-9, Mizolastine 110588-56-2,  
 Noberastine 150756-35-7, Eflétirizine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (co-administration; preparation of 1-(4-piperidinyl)benzimidazolones as  
 histamine H3 antagonists for use in combination with an  
 H1 receptor antagonists)

L3 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2003:855801 CAPLUS  
 DN 139:350734  
 TI Preparation of 1-(4-piperidinyl)benzimidazoles as histamine H3 antagonists  
 IN Zeng, Qingbei; Aslanian, Robert G.; Berlin, Michael Y.; Boyce, Christopher  
 W.; Cao, Jianhua; Kozlowski, Joseph A.; Mangiaracina, Pietro; McCormick,  
 Kevin D.; Mutahi, Mwangi W.; Rosenblum, Stuart B.; Shih, Neng-Yang;  
 Solomon, Daniel M.; Tom, Wing C.  
 PA Schering Corporation, USA  
 SO PCT Int. Appl., 132 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003088967	A1	20031030	WO 2003-US11672	20030416
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU,				
	ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD,				
	MG, MK, MN, MX, MZ, NI, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG,				
	SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				
	KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				
	FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,				
	BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2481940	AA	20031030	CA 2003-2481940	20030416
	AU 2003223627	A1	20031103	AU 2003-223627	20030416
	US 2004097483	A1	20040520	US 2003-417391	20030416
	US 7105505	B2	20060912		
	EP 1499316	A1	20050126	EP 2003-719766	20030416
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003009348	A	20050301	BR 2003-9348	20030416
	CN 1658874	A	20050824	CN 2003-813779	20030416
	JP 2005529116	T2	20050929	JP 2003-585719	20030416
	ZA 2004007984	A	20051018	ZA 2004-7984	20041004
	NO 2004005002	A	20050118	NO 2004-5002	20041117
PRAI	US 2002-373731P	P	20020418		
	US 2002-373467P	P	20020418		
	WO 2003-US11672	W	20030416		

OS MARPAT 139:350734

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The title compds. [I; R1 = (un)substituted benzimidazolyl or a derivative thereof; R2 = (un)substituted aryl or heteroaryl; M1, M2 = CR3, N; X = a bond, alkylene; Y = CO, CS, SO2, etc.; Z = a bond, alkylene, CO, etc.; R3 = H, halo, alkyl, etc.; R12 = alkyl, OH, alkoxy, etc.; R13 = alkyl, alkoxy, OH, etc.; a, b = 0-2; n, p = 1-3; r = 0-3; with the provisos] which are histamine H3 antagonists, were prepared E.g., a multi-step synthesis of II which showed Ki of 1 nM in rHu H3 binding assay, was given. Also disclosed are pharmaceutical compns. comprising the compds. of formula I and methods of treating various diseases or conditions, such as allergy, allergy-induced airway responses, and congestion (e.g., nasal congestion) using the compds. I. Also disclosed are methods of treating said diseases or

conditions using the compds. of formula I in combination with an H1 receptor antagonist.

ST piperidinybenzimidazole prepn histamine H3 antagonist allergy inhibitor; benzimidazole piperidiny prepn antihistamine H3

IT Allergy inhibitors  
 Anti-Alzheimer's agents  
 Antihistamines  
 Antihypotensives  
 Antimigraine agents  
 Antiobesity agents  
 Antipsychotics  
 Cardiovascular agents  
 Human  
 Nervous system agents  
 Nervous system depressants  
 (preparation of 1-(4-piperidiny)benzimidazoles as histamine H3 antagonists)

IT Respiratory system  
 (treatment of allergy-induced airway responses; preparation of 1-(4-piperidiny)benzimidazoles as histamine H3 antagonists)

IT Allergy  
 Alzheimer's disease  
 Cardiovascular system, disease  
 Central nervous system, disease  
 Digestive tract, disease  
 Hypotension  
 Obesity  
 Schizophrenia  
 Sleep disorders  
 (treatment of; preparation of 1-(4-piperidiny)benzimidazoles as histamine H3 antagonists)

IT 58-73-1, Diphenhydramine 59-33-6, Pyrillamine maleate 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6, Brompheniramine 91-81-6, Tripeleennamine 113-92-8, Chlorpheniramine maleate 129-03-3, Cyproheptadine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 562-10-7 569-65-3, Meclizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 15686-51-8, Clemastine 24219-97-4, Mianserin 29216-28-2, Mequitazine 34580-13-7, Ketotifen 39577-19-0, Picumast 50679-08-8, Terfenadine 58581-89-8, Azelastine 68844-77-9, Astemizole 75970-99-9, Norastemizole 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7, Epinastine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 90729-42-3, Carebastine 90729-43-4, Ebastine 100643-71-8, Descarboethoxyloratadine 108612-45-9, Mizolastine 110588-56-2, Noberastine 150756-35-7, Efletirizine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (H1 receptor antagonist; preparation of 1-(4-piperidiny)benzimidazoles as histamine H3 antagonists for use in combination with an H1 receptor antagonist)

L3 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:716267 CAPLUS

DN 137:247716

TI Preparation and use of substituted piperazine/piperidine derivatives as H receptor antagonists

IN Rosenblum, Stuart B.; Zeng, Qingbei; Mutahi, Mwangi Wa; Aslanian, Robert G.; Ting, Pauline C.; Shih, Neng-Yang; Solomon, Daniel M.; Cao, Jianhua; Vaccaro, Henry A.; McCormick, Kevin D.; Baldwin, John J.; Li, Ge

PA Schering Corporation, USA; Pharmacopeia, Inc.

SO PCT Int. Appl., 112 pp.  
 CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002072570	A2	20020919	WO 2002-US7106	20020311
	WO 2002072570	A3	20030306		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2440559	AA	20020919	CA 2002-2440559	20020311
	US 2003109564	A1	20030612	US 2002-95134	20020311
	US 6849621	B2	20050201		
	EP 1373251	A2	20040102	EP 2002-709808	20020311
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	CN 1496362	A	20040512	CN 2002-806561	20020311
	JP 2004520435	T2	20040708	JP 2002-571486	20020311
	US 2005113383	A1	20050526	US 2004-974329	20041027
PRAI	US 2001-275417P	P	20010313		
	US 2002-95134	A3	20020311		
	WO 2002-US7106	W	20020311		
OS	MARPAT 137:247716				
AB	Title compds. I [R = (hetero)aryl, heterocycloalkyl, alkyl, carboxamido, etc.; X = alkyl, S(O)2; Y = bond, CO, CS, alkyl, amido, etc.; M = C, N; Z = alkyl, SO2, CO, carboxamido; R = 5-6 membered heteroaryl, alkyl, aryl, etc.; R = alkyl, OH, alkoxy, F, etc.; n, p, q = 1-3; with some provisions] were prepared For instance, 2,5-dimethylpiperazine was alkylated with 2-bromobenzaldehyde (CH2Cl2, NaHB(OAc)3) and subsequently acylated with N-Boc-isonipecotic acid (CH2Cl2, PyBOP, i-Pr2NEt). The resulting intermediate was deprotected and reductively alkylated with pyridine-4-carboxaldehyde to afford. Selected example compds. had Ki within 0.2 and 600 nM for the H3 receptor. : I, alone and in combination with a H1 receptor antagonist, are used for the treatment of various diseases or conditions, such as, allergy, allergy-induced airway responses and congestion (e.g., nasal congestion).				
ST	piperazine piperidine h1 h3 receptor antagonist prepn				
IT	Allergy Allergy inhibitors Alzheimer's disease Anti-Alzheimer's agents Antimigraine agents Antiobesity agents Cardiovascular agents Cardiovascular system, disease Digestive tract Human Hypotension Nervous system agents Obesity Schizophrenia Sleep disorders (preparation and use of substituted piperazine/piperidine derivs. as H receptor antagonists)				
IT	58-73-1, Diphenhydramine	59-33-6	60-87-7, Promethazine	68-88-2, Hydroxyzine	82-92-8, Cyclizine
	84-96-8, Trimeprazine	86-22-6, Brompheniramine	91-81-6, Tripeleminamine	113-92-8, Chlorpheniramine	129-03-3, Cyproheptadine
	486-12-4, Triprolidine	486-16-8, Carbinoxamine	562-10-7	569-65-3, Meclizine	3964-81-6, Azatadine
	5636-83-9, Dimethindene	15686-51-8, Clemastine	24219-97-4, Mianserin	29216-28-2, Mequitazine	34580-13-7, Ketotifen
	39577-19-0, Picumast				

50679-08-8, Terfenadine 58581-89-8, Azelastine 68844-77-9, Astemizole  
 75970-99-9, Norastemizole 79516-68-0, Levocabastine 79794-75-5,  
 Loratadine 80012-43-7, Epinastine 83799-24-0, Fexofenadine  
 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine  
 90729-42-3, Carebastine 90729-43-4, Ebastine 100643-71-8,  
 Descarboethoxyloratadine 108612-45-9, Mizolastine 110588-56-2,  
 Noberastine 150756-35-7, Eflétirizine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (combination pharmaceutical; preparation and use of substituted  
 piperazine/piperidine derivs. as H receptor antagonists)

L3 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2002:314934 CAPLUS  
 DN 136:340592  
 TI Preparation of 4-[4-(piperidin-1-ylcarbonyl)piperidin-1-ylmethyl]pyridin-2-  
 ylamines as antagonists of histamine H3 receptors  
 IN Aslanian, Robert G.; Shih, Neng-Yang; Ting, Pauline C.; Berlin, Michael  
 Y.; Rosenblum, Stuart B.; McCormick, Kevin D.; Tom, Wing C.; Boyce,  
 Christopher W.; Mangiaracina, Pietro; Mutahi, Mwangi Wa; Piwinski, John J.  
 PA Schering Corporation, USA  
 SO PCT Int. Appl., 144 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002032893	A2	20020425	WO 2001-US32151	20011015
	WO 2002032893	A3	20020822		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU,				
	ID, IL, IN, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LU, LV, MA,				
	MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI,				
	SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				
	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				
	BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2424664	AA	20020425	CA 2001-2424664	20011015
	AU 2002015355	A5	20020429	AU 2002-15355	20011015
	US 2003045519	A1	20030306	US 2001-978267	20011015
	US 6720328	B2	20040413		
	BR 2001014754	A	20030701	BR 2001-14754	20011015
	EP 1326858	A2	20030716	EP 2001-983968	20011015
	EP 1326858	B1	20051214		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	CN 1469873	A	20040121	CN 2001-817512	20011015
	HU 200303835	A2	20040301	HU 2003-3835	20011015
	JP 2004511553	T2	20040415	JP 2002-536275	20011015
	NZ 524857	A	20041224	NZ 2001-524857	20011015
	EP 1571145	A1	20050907	EP 2005-9405	20011015
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, FI, RO, CY, TR				
	AT 312833	E	20051215	AT 2001-983968	20011015
	ES 2250500	T3	20060416	ES 2001-1983968	20011015
	CN 1803795	A	20060719	CN 2005-10131094	20011015
	ZA 2003002521	A	20040630	ZA 2003-2521	20030331
	NO 2003001744	A	20030614	NO 2003-1744	20030415
	HK 1052935	A1	20060519	HK 2003-105161	20030717
	US 2004097513	A1	20040520	US 2003-699189	20031031
PRAI	US 2000-240901P	P	20001017		
	CN 2001-817512	A3	20011015		
	EP 2001-983968	A3	20011015		
	US 2001-978267	A3	20011015		



OS MARPAT 136:340592

AB The title compds. [I; R1 = (un)substituted aryl, heteroaryl, alkyl, etc.; X = CO, C(NOR3), C(MNR4R5), etc.; M1 = C; M2 = C, N; M3, M4 = C, N; Y = CH2, CO, C(NOH), etc.; Z = alkyl; R2 = (un)substituted 5-6 membered heteroaryl; R3 = H, alkyl, aryl, etc.; R4 = H, alkyl, aryl, etc.; R5 = H, alkyl, COR4, etc.; R12, R13 = alkyl, OH, alkoxy, F; a, b = 0-2; n, p = 1-3, with the proviso that when M3 and M4 are both N atoms, then p = 2 or 3], useful in treating various diseases or conditions, such as, for example, allergy, allergy-induced airway responses, and congestion (e.g., nasal congestion), were prepared. E.g., a multi-step synthesis of II which showed Ki of 0.83 nM in H3 receptor binding assay, was given. Also disclosed are methods of treating various diseases or conditions, such as, for example, allergy, allergy-induced airway responses, and congestion (e.g., nasal congestion) using the compds. I in combination with a H1 receptor antagonist.

ST antihistamine H3 piperidinylcarbonylpiperidinylmethylpyridinylamine prepn; histamine H3 antagonist piperidinylcarbonylpiperidinylmethylpyridinylamine prepn; allergy inhibitor piperidinylcarbonylpiperidinylmethylpyridinylamine prepn; nasal decongestant piperidinylcarbonylpiperidinylmethylpyridinylamine prepn

IT Allergy inhibitors  
Anti-Alzheimer's agents  
Antiobesity agents  
Cardiovascular agents  
Nervous system stimulants

(preparation of 4-[4-(piperidin-1-ylcarbonyl)piperidin-1-ylmethyl]pyridin-2-ylamines as antagonists of histamine H3 receptors)

IT 58-73-1, Diphenhydramine 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6, Brompheniramine 91-81-6, Tripeleminamine 91-84-9, Pyrilamine 129-03-3, Cyproheptadine 132-22-9, Chlorpheniramine 469-21-6, Doxylamine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 569-65-3, Meclizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 15686-51-8, Clemastine 24219-97-4, Mianserin 29216-28-2, Mequitazine 34580-13-7, Ketotifen 39577-19-0, Picumast 50679-08-8, Terfenadine 68844-77-9, Astemizole 75970-99-9, Norastemizole 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7, Epinastine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 90729-42-3, Carebastine 90729-43-4, Ebastine 100643-71-8, Descarboethoxyloratadine 108612-45-9, Mizolastine 110588-56-2, Noberastine 150756-35-7, Efletirizine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(H1 receptor antagonist; preparation of 4-[4-(piperidin-1-ylcarbonyl)piperidin-1-ylmethyl]pyridin-2-ylamines as antagonists of histamine H3 receptors)

L3 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:360990 CAPLUS

DN 136:48247

TI Histamine H3 antagonists

AU McLeod, Robbie L.; Egan, Robert W.; Cuss, Francis M.; Bolser, Donald C.; Hey, John A.

CS Allergy, Schering-Plough Research Institute, Kenilworth, NJ, USA

SO Progress in Respiratory Research (2001), 31(New Drugs for Asthma, Allergy and COPD), 133-136

CODEN: PRRRAE; ISSN: 1422-2140

PB S. Karger AG

DT Journal

LA English

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Treatment of allergic rhinitis often involves the use of

H1 antihistamines which block histamine, a primary mediator in allergic responses. Antihistamines alone do not provide significant benefit against the congestion associated with allergic rhinitis and are commonly given in combination with  $\alpha$ -adrenergic decongestants. Whereas these decongestants are effective in reducing the congestion associated with allergic nasal disease, they may produce undesirable side effects, such as hypertension, agitation, and insomnia. Presently, the authors discuss preclin. findings showing that combination histamine H1 and H3 receptor blockade produces decongestant activity without the hypertensive liability characteristic of  $\alpha$ -adrenoceptor agonists.

ST antihistamine H3 decongestant allergic rhinitis

IT Histamine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(H1; histamine H1/H3 antagonists in  
allergic rhinitis)

IT Antihistamines

(H3; histamine H1/H3 antagonists in  
allergic rhinitis)

IT Histamine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(H3; histamine H1/H3 antagonists in  
allergic rhinitis)

IT Allergy

Inflammation

Nose, disease

(allergic rhinitis; histamine H1/H3  
antagonists in allergic rhinitis)

IT Blood pressure

(histamine H1/H3 antagonists in allergic  
rhinitis)

IT Decongestants

(nasal; histamine H1/H3 antagonists in  
allergic rhinitis)

IT Circulation

(regional, nose; histamine H1/H3 antagonists in  
allergic rhinitis)

IT 106243-16-7, Thioperamide 145231-45-4, Clobenpropit

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(combined with chlorpheniramine; histamine H1/H3  
antagonists in allergic rhinitis)

IT 113-92-8 79794-75-5, Loratadine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(combined with thioperamide; histamine H1/H3  
antagonists in allergic rhinitis)

L3 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:167001 CAPLUS

DN 134:247322

TI Cloning and pharmacological characterization of a fourth histamine  
receptor (H4) expressed in bone marrow

AU Liu, Changlu; Ma, Xiao-Jun; Jiang, Xiaoxia; Wilson, Sandy J.; Hofstra,  
Claudia L.; Blevitt, Jonathan; Pyati, Jayashree; Li, Xiaobing; Chai,  
Wenying; Carruthers, Nicholas; Lovenberg, Timothy W.

CS The R. W. Johnson Pharmaceutical Research Institute, San Diego, CA, USA

SO Molecular Pharmacology (2001), 59(3), 420-426

CODEN: MOPMA3; ISSN: 0026-895X

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Histamine is a multifunctional hormone that regulates smooth muscle contraction in the airways, acid secretion in the gut, and neurotransmitter release in the central nervous system through three well characterized receptor subtypes, H1, H2, H3, resp. As part of a directed effort to discover novel G-protein-coupled receptors through homol. searching of genomic databases, the authors identified a partial clone (GPCR105) that had significant homol. to the recently identified histamine H3 receptor cDNA. Expression of the full-length human GPCR105 in cells confers the ability to bind [3H]histamine with high affinity ( $K_D = 5$  nM). GPCR105 is pharmacol. similar to the histamine H3 receptor in that it binds many of the known H3 agonists and antagonists, albeit with a different rank order of affinity/potency. GPCR105 does not bind (i.e.,  $K_D > 10$   $\mu$ M) all tested H1 and H2 receptor antagonists such as diphenhydramine, loratadine, ranitidine, and cimetidine, but has modest affinity for the H2 receptor agonist, dimaprit (377 nM). Whereas the H3 receptor is expressed almost exclusively in nervous tissues, GPCR105 is expressed primarily in bone marrow and eosinophils. Together, these data demonstrate that GPCR105 is a novel histamine receptor structurally and pharmacol. related to the H3 receptor. However, its unique expression profile and physiol. role suggest that GPCR105 is a fourth histamine receptor subtype (H4) and may be a therapeutic target for the regulation of immune function, particularly with respect to allergy and asthma.

L3 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2000:567449 CAPLUS  
 DN 133:168392  
 TI Composition and method for treating allergic diseases  
 IN Aslanian, Robert G.; Piwinski, John J.  
 PA Schering Corporation, USA  
 SO U.S., 9 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6103735	A	20000815	US 1999-412621	19991006
PRAI	US 1999-412621		19991006		
OS	MARPAT 133:168392				

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Composition and method for treating allergic diseases  
 AB The present invention is directed towards a pharmaceutical composition useful for the treatment of allergic rhinitis, asthma and related disorders. In one embodiment, the composition comprises, in combination, a therapeutically effective amount of at least one neurokinin antagonist, a therapeutically effective amount of at least one H3 antagonist and a therapeutically effective amount of at least one H1 antagonist.  
 ST neurokinin histamine antagonist combination allergy treatment  
 IT Antihistamines  
     (H1; antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)  
 IT Antihistamines  
     (H3; antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)  
 IT Nose  
     (allergic rhinitis; antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)  
 IT Antitussives  
     Asthma  
     Decongestants  
     Drug delivery systems

# Expectorants

(antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)

## IT Neurokinins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(antagonists; antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)

## IT Nose

(congestion; antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)

## IT Respiratory tract

(disease; antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)

## IT Eye

(redness; antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)

## IT Breathing (animal)

(wheezing; antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)

IT 59-33-6, Pyrillamine 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6, Brompheniramine 91-81-6, Tripeleminamine 113-92-8, Chlorpheniramine 129-03-3, Cyproheptadine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 562-10-7, Doxylamine 569-65-3, Mecizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 5786-21-0, Clozapine 15686-51-8, Clemastine 24219-97-4, Mianserin 29216-28-2, Mequitazine 34580-13-7, Ketotifen 34970-69-9, Burimamide 34973-91-6, Impentamine 39577-19-0, Picumast 46129-28-6, SKF-91486 50679-08-8, Terfenadine 55273-05-7, Impromidine 58581-89-8, Azelastine 68844-77-9, Astemizole 75970-99-9, Norastemizole 79313-75-0, Sopromidine 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7, Epinastine 83184-43-4, Mifentidine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 90729-42-3, Carebastine 90729-43-4, Ebastine 99616-14-5, S-Sopromidine 100643-71-8, Descarboethoxyloratadine 106243-16-7, Thioperamide 108612-45-9, Mizolastine 110588-56-2, Noberastine 145231-45-4, Clobenpropit 150756-35-7, Eftirizine 152030-16-5, UCL 1199 152241-24-2, GT-2016 176860-26-7, GR-175737 213027-19-1, GT-2331 224585-45-9 263892-22-4 263892-24-6 263892-25-7 263892-26-8  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antagonists of neurokinin receptors and histamine receptors for treating allergic diseases)

L3 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:259985 CAPLUS

DN 132:284236

TI Composition and method for treating allergic diseases

IN Aslanian, Robert G.; Piwinski, John J.

PA Schering Corporation, USA

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000021512	A2	20000420	WO 1999-US21437	19991006
	WO 2000021512	A3	20000706		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ,			

PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ,  
 VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2346227	AA	20000420	CA 1999-2346227	19991006
AU 9962526	A1	20000501	AU 1999-62526	19991006
EP 1117405	A2	20010725	EP 1999-949707	19991006

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO

JP 2002527381	T2	20020827	JP 2000-575488	19991006
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PRAI US 1998-169608	A	19981009
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WO 1999-US21437	W	19991006
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OS MARPAT 132:284236

TI Composition and method for treating allergic diseases

AB The present invention is directed towards a pharmaceutical composition useful for the treatment of allergic rhinitis, asthma and related disorders. In one embodiment, the compns. comprise, in combination, a therapeutically effective amount of at least one neurokinin antagonist, a therapeutically effective amount of at least one H3 antagonist and a therapeutically effective amount of at least one H1 antagonist. The invention neurokinin antagonists include 3,5-dichloro-N-[3-(3,4-dichlorophenyl)-2-(methoxyimino)-5-(2-oxo[1,4'-bipiperidin]-1'-yl)pentyl]-N-methylbenzamide and derivs. thereof.

ST piperidinoalkoximinopentylbenzamide analog neurokinin antagonist  
 antihistaminic allergy

IT Antihistamines

(H1; pharmaceutical compns. containing neurokinin antagonists and antihistaminics for treatment of allergic diseases)

IT Antihistamines

(H3; pharmaceutical compns. containing neurokinin antagonists and antihistaminics for treatment of allergic diseases)

IT Nose

(allergic rhinitis; pharmaceutical compns. containing neurokinin antagonists and antihistaminics for treatment of allergic diseases)

IT Neurokinins

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (antagonists; pharmaceutical compns. containing neurokinin antagonists and antihistaminics for treatment of allergic diseases)

IT Nose

(congestion; pharmaceutical compns. containing neurokinin antagonists and antihistaminics for treatment of allergic diseases)

IT Allergy inhibitors

Asthma

Cough

Drug delivery systems

(pharmaceutical compns. containing neurokinin antagonists and antihistaminics for treatment of allergic diseases)

IT Eye, disease

(redness; pharmaceutical compns. containing neurokinin antagonists and antihistaminics for treatment of allergic diseases)

IT Breathing (animal)

(wheezing; pharmaceutical compns. containing neurokinin antagonists and antihistaminics for treatment of allergic diseases)

IT 59-33-6, Pyrilamine 60-87-7, Promethazine 68-88-2, Hydroxyzine

82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6 91-81-6,

Tripelennamine 113-92-8 129-03-3, Cyproheptadine 486-12-4,

Tripolidine 486-16-8, Carbinoxamine 562-10-7, Doxylamine 569-65-3,

Meclizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 5786-21-0,

Clozapine 15686-51-8, Clemastine 24219-97-4, Mianserin 29216-28-2,

Mequitazine 34580-13-7, Ketotifen 34970-69-9, Burimamide 34973-91-6,

Impentamine 39577-19-0, Picumast 46129-28-6, SKF-91486 50679-08-8,

Terfenadine 55273-05-7, Impromidine 58581-89-8, Azelastine

68844-77-9, Astemizole 75970-99-9, Norastemizole 79313-75-0  
 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7,  
 Epinastine 83184-43-4, Mifentidine 83799-24-0, Fexofenadine  
 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine  
 90729-42-3, Carebastine 90729-43-4, Ebastine 99616-14-5, S-Sopromidine  
 100643-71-8, Descarboethoxyloratadine 106243-16-7, Thioperamide  
 108612-45-9, Mizolastine 110588-56-2, Noberastine 145231-45-4,  
 Clobenpropit 150756-35-7, Eflerizine 152030-16-5, UCL 1199  
 152241-24-2, GT-2016 176860-26-7, GR-175737 213027-19-1, GT-2331  
 224585-45-9 226915-31-7 226915-78-2 226916-77-4 263892-22-4  
 263892-24-6 263892-25-7 263892-26-8 263892-27-9 263892-28-0  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)

(pharmaceutical compns. containing neurokinin antagonists and  
 antihistaminics for treatment of allergic diseases)

L3 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1999:104511 CAPLUS

DN 130:163188

TI Treatment of upper airway allergic responses with H1-  
 and H3-histamine receptor antagonists

IN Kreutner, William; Hey, John A.

PA Schering Corporation, USA

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5869479	A	19990209	US 1997-909319	19970814
PRAI	US 1997-909319		19970814		

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Treatment of upper airway allergic responses with H1-  
 and H3-histamine receptor antagonists

AB Relief from the symptoms of rhinitis is obtained by treatment with: (a) an  
 antihistaminic effective amount of a histamine H1 receptor  
 antagonist; together with (b) a sufficient amount of a histamine H3  
 receptor antagonist to provide a nasal decongestant effect. The  
 components may be administered together in a single dosage form, or sep.  
 in the same or different dosage forms to maintain therapeutic systemic  
 levels of both components.

ST H1 H3 histamine antagonist rhinitis; upper airway  
 allergy histamine receptor antagonist

IT Antihistamines

Blood pressure

Decongestants

Drug delivery systems

Drug interactions

(H1- and H3-histamine receptor antagonists for  
 treatment of rhinitis)

IT Antihistamines

(H1; H1- and H3-histamine receptor  
 antagonists for treatment of rhinitis)

IT Histamine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(H3, antagonists; H1- and H3-histamine  
 receptor antagonists for treatment of rhinitis)

IT Drug delivery systems

(capsules; H1- and H3-histamine receptor  
 antagonists for treatment of rhinitis)

IT Drug delivery systems

Drug delivery systems  
(ligs., oral; H1- and H3-histamine receptor antagonists for treatment of rhinitis)

IT Drug delivery systems  
(parenterals; H1- and H3-histamine receptor antagonists for treatment of rhinitis)

IT Nose  
(rhinitis; H1- and H3-histamine receptor antagonists for treatment of rhinitis)

IT Drug delivery systems  
(tablets; H1- and H3-histamine receptor antagonists for treatment of rhinitis)

IT 154-41-6, Phenylpropanolamine hydrochloride 150036-88-7, Verongamine  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(H1- and H3-histamine receptor antagonists for treatment of rhinitis)

IT 58-73-1, Diphenhydramine 59-33-6 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6, Brompheniramine 91-81-6, Tripeleminamine 113-92-8, Chlorpheniramine maleate 129-03-3, Cyproheptadine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 523-87-5, Dimenhydrinate 562-10-7 569-65-3, Meclizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 5786-21-0, Clozapine 15686-51-8, Clemastine 24219-97-4, Mianserin 29216-28-2, Mequitazine 34580-13-7, Ketotifen 34970-69-9, Burimamide 34973-91-6, Impentamine 39577-19-0, Picumast 46129-28-6, SKF-91486 50679-08-8, Terfenadine 55273-05-7, Impromidine 58581-89-8, Azelastine 68844-77-9, Astemizole 75970-99-9, Norastemizole 79313-75-0, Sopromidine 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7, Epinastine 83184-43-4, Mifentidine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 90729-42-3, Carebastine 90729-43-4, Ebastine 99616-14-5, S-Sopromidine 100643-71-8, Descarboethoxyloratadine 106243-16-7, Thioperamide 108612-45-9, Mizolastine 110588-56-2, Noberastine 145231-45-4, Clobenpropit 148440-81-7 150756-35-7, Efletirizine 152241-24-2, GT-2016 176860-26-7, GR 175737  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(H1- and H3-histamine receptor antagonists for treatment of rhinitis)

IT 152030-16-5  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(UCL 1199; H1- and H3-histamine receptor antagonists for treatment of rhinitis)

L3 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1998:202807 CAPLUS  
DN 128:229269  
TI Histamine in the pathogenesis of asthma  
AU Akagi, Masaaki  
CS Fac. Pharm. Sci., Tokushima Bunri Univ., Tokushima, 770-8514, Japan.  
SO Nippon Yakurigaku Zasshi (1998), 111(4), 217-222  
CODEN: NYKZAU; ISSN: 0015-5691  
PB Nippon Yakuri Gakkai  
DT Journal; General Review  
LA Japanese  
AB A review with 47 refs. While it is clear that the clin. expression of IgE-mediated diseases depends upon the actions of multiple mediators, histamine, the earliest recognized mediator of allergy, remains a prominent contributor. Histamine released from mast cells binds to specific receptors (H1, H2, H3) to produce its clin.

effects. The cardinal features of asthma include smooth muscle spasm, mucosal edema, inflammation, and mucus secretion. It has been demonstrated that 2 of these features, bronchospasm and mucosal edema, can be caused by H1-receptor stimulation, while H2- and possibly H1-activation are probably minor causes of mucus secretion. Histamine interacts directly with the endothelial cells (EC) and induces permeability, a transient expression of P-selectin and the secretion of lipid mediators (e.g. PGI2, PAF and LTB4). Moreover, histamine induces a significant increase of IL-6 and IL-8 secretion by EC. Since IL-8 exerts a chemotactic activity for neutrophils, eosinophils, and basophils, and IL-6 is involved in endothelium permeability, the secretion of cytokines may be involved in the late phase reaction. Some antihistamines (i.e., levocabastine, terfenadine, loratadine, azelastine, and oxatamide) can reduce ICAM-1 expression. The participation of histamine in the allergic inflammation, including asthma, must be re-examined, since the effects of histamine are more widespread.

L3 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1998:124005 CAPLUS

DN 128:208908

TI Treatment of upper airway allergic responses with a combination of histamine receptor antagonists

IN Kreutner, William; Hey, John A.

PA Schering Corporation, USA

SO PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9806394	A1	19980219	WO 1997-US13903	19970813
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	ZA 9707263	A	19980216	ZA 1997-7263	19970813
	CA 2263163	AA	19980219	CA 1997-2263163	19970813
	AU 9739733	A1	19980306	AU 1997-39733	19970813
	AU 722040	B2	20000720		
	EP 920315	A1	19990609	EP 1997-937153	19970813
	EP 920315	B1	20051228		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI, RO				
	BR 9711149	A	19990817	BR 1997-11149	19970813
	CN 1233179	A	19991027	CN 1997-198713	19970813
	JP 2000505094	T2	20000425	JP 1998-509859	19970813
	JP 3638289	B2	20050413		
	NZ 334063	A	20000929	NZ 1997-334063	19970813
	HU 9904362	A2	20001128	HU 1999-4362	19970813
	JP 2003095979	A2	20030403	JP 2002-222138	19970813
	TW 221768	B1	20041011	TW 1997-86111627	19970813
	AT 314071	E	20060115	AT 1997-937153	19970813
	PL 191073	B1	20060331	PL 1997-331617	19970813
	KR 2000029975	A	20000525	KR 1999-701226	19990212
	NO 9900706	A	19990215	NO 1999-706	19990215
PRAI	US 1996-689951	A	19960816		
	JP 1998-509859	A3	19970813		
	WO 1997-US13903	W	19970813		

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Treatment of upper airway allergic responses with a combination



of histamine receptor antagonists

AB Relief from the symptoms of rhinitis is obtained by treatment with: (a) an antihistaminic effective amount of a histamine H1 receptor antagonist; together with (b) a sufficient amount of a histamine H3 receptor antagonist to provide a nasal decongestant effect. The components may be administered together in a single dosage form, or sep. in the same or different dosage forms to maintain therapeutic systemic levels of both components. The nasal airways resistance following injection of 3 mg/kg loratadine and 10 mg/kg thioperamide in cats was 2.1 as compared with 10.2 for loratadine alone. A tablet contained H1 antagonist effective amount, H3 antagonist effective amount, lactose 100, 10% corn starch past 5, dried corn starch 25, and magnesium stearate 1.25 mg.

ST upper airway allergy histamine receptor antagonist;  
loratadine thioperamide nasal decongestant tablet

IT Antihistamines

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(H1; treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT Histamine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (H3, antagonist; treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT Drug delivery systems

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(capsules; treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT Drug delivery systems

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(liqs., oral; treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT Decongestants

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nasal; treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT Drug delivery systems

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(parenterals, solns.; treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT Nose

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(rhinitis; treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT Drug delivery systems

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tablets; treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT Antihistamines

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT Respiratory tract

(upper; treatment of upper airway allergic responses with combination of histamine receptor antagonists)

IT 58-73-1, Diphenhydramine 59-33-6 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-92-8, Cyclizine 84-96-8, Trimeprazine 86-22-6 91-81-6, Tripeleminamine 113-92-8 129-03-3, Cyproheptadine 486-12-4, Triprolidine 486-16-8, Carbinoxamine 523-87-5, Dimenhydrinate 562-10-7 569-65-3, Meclizine 3964-81-6, Azatadine 5636-83-9, Dimethindene 5786-21-0, Clozapine 14838-15-4, Phenylpropanolamine 15686-51-8, Clemastine 24219-97-4, Mianserin 29216-28-2, Mequitazine 34580-13-7, Ketotifen 34970-69-9, Burimamide 39577-19-0, Picumast 46129-28-6, Skf-91486 50679-08-8, Terfenadine 55273-05-7, Impromidine 58581-89-8, Azelastine 68844-77-9, Astemizole 75970-99-9, Norastemizole 79313-75-0, Sopromidine 79516-68-0, Levocabastine 79794-75-5, Loratadine 80012-43-7, EPinastine 83184-43-4, Mifentidine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 90729-42-3, Carebastine 90729-43-4, Ebastine 99616-14-5, S-Sopromidine 100643-71-8, Descarboethoxyloratadine 106243-16-7, Thioperamide 108612-45-9, Mizolastine 110588-56-2, Noberastine 145231-45-4, Clobenpropit 150036-88-7, Verongamine 150756-35-7, Eflétirizine 152030-16-5, UCL 1199 152241-24-2, Gt-2016 176860-26-7, GR 175737  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of upper airway allergic responses with combination of histamine receptor antagonists)

L3 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1995:521009 CAPLUS

DN 122:306242

TI Pharmacological studies of allergic cough in the guinea pig

AU Bolser, Donald C.; DeGennaro, Frances C.; O'Reilly, Sandra; Hey, John A.; Chapman, Richard W.

CS 2015 Galloping Hill Road, Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA

SO European Journal of Pharmacology (1995), 277(2/3), 159-64  
CODEN: EJPHAZ; ISSN: 0014-2999

PB Elsevier

DT Journal

LA English

TI Pharmacological studies of allergic cough in the guinea pig

AB The pharmacol. mechanisms of allergic cough in the guinea pig were studied. Actively sensitized guinea pigs were exposed to aerosols of antigen to elicit coughing. In sep. expts., naive guinea pigs were exposed to aerosols of capsaicin to elicit coughing. Both allergic and capsaicin-induced coughs were inhibited by loratadine (0.3-10 mg/kg orally) and chlorpheniramine (0.1-3.0 mg/kg orally). Neither cimetidine (10 mg/kg s.c.) nor thioperamide (3-10 mg/kg s.c.) inhibited allergic or capsaicin-induced cough. Codeine (3-30 mg/kg orally), salbutamol (0.003-3.0 mg/kg s.c.) and ipratropium (0.03-1.0 mg/kg s.c.) inhibited both allergic and capsaicin-induced cough. Hexamethonium (10 and 30 mg/kg s.c.) inhibited allergic, but not capsaicin-induced, cough. Allergic and capsaicin-induced coughs were unaffected by phenidone (5.0 and 10.0 mg/kg s.c.). Indomethacin (5.0 and 10.0 mg/kg s.c.) had no effect on allergic cough but slightly inhibited capsaicin-induced cough. It is concluded that allergic and capsaicin-induced coughs are modulated by histamine H1 receptor and cholinergic mechanisms. Histamine H2 or histamine H3 receptor mechanisms, and lipoxygenase and cyclooxygenase products of arachidonic acid metabolism, do

not influence allergic and capsaicin-induced cough. Ganglionic mechanisms play a minor role in the production of allergic cough and no role in capsaicin-induced cough.

ST cough mechanism pharmacol; allergy cough mechanism pharmacol; capsaicin cough mechanism pharmacol

IT Antitussives

(allergic and capsaicin-induced cough response to)

IT Allergy

Cough

(mechanisms and pharmacol. of allergic cough and capsaicin-induced cough)

IT Neurotransmission

(cholinergic, mechanisms of allergic and capsaicin-induced cough involving)

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (histaminic H1, mechanisms of allergic and capsaicin-induced cough involving)

IT 53-86-1, Indomethacin 55-97-0, Hexamethonium bromide 76-57-3, Codeine 92-43-3, Phenidone 113-92-8, Chlorpheniramine maleate 18559-94-9, Salbutamol 22254-24-6, Ipratropium bromide 51481-61-9, Cimetidine 79794-75-5, Loratadine 106243-16-7, Thioperamide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(allergic and capsaicin-induced cough response to)

IT 39391-18-9, Cyclooxygenase 63551-74-6, Lipoxxygenase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (mechanisms of allergic and capsaicin-induced cough involving)

IT 506-32-1, Arachidonic acid

RL: BSU (Biological study, unclassified); BIOL (Biological study) (mechanisms of allergic and capsaicin-induced cough involving metabolism of)